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KALA AZAR IN MADRAS

C. DONOVAN

Transactions of the Bombay Medical Congress, 1909.

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TRANSACTIONS BOMBAY MEDICAL CONGRESS, 1909.

KALA AZAR IN MADRAS.

By Major C. DONOVAN, I.M.S.,
Second Physician, General Hospital, Madras.

In the paper I intend to read to you to-day, I shall not attempt to go over all the facts relating to this disease, most of these are well known, but shall limit myself to certain factors not generally recognised by the majority of observers investigating tropical diseases.

I shall take up the following four heads :—

I—The nature of the parasite.
II—The mode of transmission of the disease.
III—The diagnosis of the disease, especially by the examination of the finger blood.
IV—Attempts at cure, by (*a*) drugs, (*b*) by bringing on inflammation and (*c*) by change of residence.

As far as the Madras Presidency is concerned the disease is very limited in its distribution, being strictly confined to the municipal boundaries of the Corporation of Madras and particularly so to the old native city, previously called Blacktown but now more euphemistically known under the appellation of Georgetown, in honour of the recent visit of His Highness the Prince of Wales.

The cases admitted from the district have, on closer investigation of their history, invariably been found to have contracted the malady within the city precincts. Kala Azar has evidently existed in Madras for a long time, it has been well-known as "Blacktown Fever" for the last 30 years at least; I remember on my first arrival in Madras now nearly 18 years ago, Col. King, the late able Sanitary Commissioner of our Presidency, speaking to me of its existence in Blacktown, and comparing it in its malignity to the dread malarial fever of Cuddapah. He considered the disease, as well as I recollect, to be a form *sui generis* and not the ordinary malaria. Up to the end of last year, I have had 379 admissions for this disease in my wards, that is, since I discovered the parasite in the spleen blood of a boy named Doraisamy, on the 16th June 1903. In addition to the above number, I have seen and examined, roughly speaking, about 150 in the wards of the other three physicians attached to the General Hospital.

This gives a total of about 530 cases that have come under my observation. Of my own admissions, there occurred 30 in the half-year 1903, 110 in 1904, 140 in 1905 (I was absent on leave in 1906), 40 in the half-year 1907 and 59 last year. The admissions for this disease do not appear to be so frequent or of so virulent a nature as previously. What the old physicians would call a "change of type" has taken place. I throw out this suggestion very guardedly, as I have not had the same number of severe cases as in previous years.

I.—Nature of the Parasite.—A considerable amount of controversy has taken place as to what position the parasite of Kala Azar should take in the order of Protozoa, but since Rogers'[1] discovery of the growth of Leishmania in citrate of sodium solution, and more so by its pullulation in the nutrient fluids of Novy[2] and more recently, of Nicolle,[3] there can be but little doubt that the organism is to be referred to the class Mastigophora or that of the flagellates, and more especially to the genus Herpetomonas. Not so much to the type species H. muscæ-domesticæ of Burnett, as to the smaller species found in the plant feeding bugs or Rhynchotes, especially to H. lygæi (Patton), found in the gut of the bug, Lygæus militaris, commonly occurring on the Milk weed, Calotropis gigantea and H. inhospes, sps. nov. found in the intestinal contents of another bug L. hospes, frequenting the pods of the Red Silk Cotton tree, Bombax malabaricum. In these Rhynchotes, stages almost identical with those of Leishmania Donovani are present in all gradations from the inert looking cockle-shaped mass, as found in man, to the long flagellated forms in citrate of sodium solution. The appearances are surprisingly alike. Patton has gone into this question in a paper which has recently appeared in the Archiv für Portistenkunde.[4] To the other herpetomonads the resemblance is not so close. I have compared them to flagellates of this genus in several flies, Sarcophaga, Calliphora, etc. The coloured plate accompanying this paper, carefully drawn by means of Abbe's camera lucida, will show at a glance the close morphological similarity I speak of.

Now, as far as I am acquainted with the parasitic flagellates, no herpetomonads are found in the gut of biting insects; flies, for instance, of the genera Hæmatopota, Tabanus and Stomoxys; Culicids like Anopheles; and bugs of predatory nature like Conorrhinus Gerris; here we have to do with the more advanced and highly organised genus Crithidia, forms approaching the trypanosomes in their complexity of structure.

There appears to be still a considerable amount of confusion, one may say ignorance of the three parasitic genera, Herpetomonas, Crithidia and Trypanosoma; all forms not in possession of an undulatory membrane and a posteriorly placed blepharoplast are loosely called "herpetomonas" forms or "wild trypanosomes" (sic). As I have had under observation during the last 18 months a number of these three genera, I may be pardoned for my presumption, in setting this question on a sounder basis.

[1] Rogers. Lancet, 23rd July 1904, p. 215.
[2] Novy and MacNeal. On the cultivation of Trypanosoma Brucei, Journal of Infectious Diseases, Vol. I, 1904, p. 1, and On the Trypanosomes of Birds. *Id.* Vol. 2, 1905, p. 256.
[3] Nicolle. Culture des corps de Leishman isolés de la rate dans trois cas d'anémie splénique infantile. Bulletin de la Soci té de Pathologie Exotique. Tome I, 1908, p. 121, and Sur trois cas d'infection splénique infantile a corps de Leishman observès en Tunisie. Archives de l'Institut Pasteur de Tunis. Fascicule I, Fevrier 1908.
[4] Patton. Herpetomonas lygæi. Archiv für Protistenkunde. Band XIII, 1908, p. 1.

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With the help of a coloured plate carefully drawn to scale, I hope I may be explicit enough to do so. The full grown form of the genus Herpetomonas is characterised by a blepharoplast placed almost at the very extreme anterior end and with no signs of an undulatory membrane. The largest forms are found in this genus, for instance, H. muscæ-domesticæ measures 70 μ to 120 μ including the flagellum. This genus occurs in the non-biting flies and plant frequenting bugs.

In Crithidia the blepharoplast is located near and anterior to the nucleus; there is also present what may be called a rudimentary undulatory membrane. The parasites of this genus are found in the gut of the biting flies in predatory and plant-frequenting bugs, in mosquitoes and in ticks. In Trypanosoma we have the blepharoplast placed at the very extreme posterior end and an undulatory membrane very well developed. These forms are parasitic in the vertebrates. These distinguishing characters are usually very well pronounced, but in the gut of some of the non-biting flies, especially in Sarcophaga, all gradations are present as far as the location of the blepharoplast is concerned; for instance, this may be anterior or posterior to or near the nucleus, the undulatory membrane, however, is always absent. (*Vide* Plate 1, Fig. 7.)

It is clear that Leishmania belongs to the first-named genus of these flagellates, and, as mentioned before, very similar to Herpetomonas lygæi and inhospes. The question then is, should we still retain the genus Leishmania for the parasite of Kala Azar or incorporate it in that of Herpetomonas. As more investigations are made amongst parasites of this group, other generic distinctions will be discovered thus necessitating a further splitting up of the genus Herpetomonas. Already an attempt[5] has been made to recreate a new genus, Leptomonas for Herpetomonas found in non-biting diptera of the genus Drosophila. These forms are very like Herpetomonas lygæi and inhospes and, as mentioned before, these two species are almost identical morphologically with Leishmania; consequently this genus may be merged in Leptomonas. But as Leishmania has, as far as is known at present, a peculiarly limited habitat, *i.e.*, restricted to mammals, we are compelled to retain this genus, not so much on morphological as on œcological grounds. The old genus Herpetomonas may be split into:—

Herpetomonas.—The type being the large flagellate, H. muscæ-domesticæ,* (Burnett)[6] occurring in the gut of the common house fly.

Leptomonas.—A smaller and slenderer form found in the gut of the plant-frequenting bugs of the genus Lygæus, etc. Type L. drosophilæ (Chatton and Alilaire).[7]

Leishmania.—The form occurring in mammals, the type being L. Donovani (Laveran and Mesnil).[8]

All this speaks against the previous views[9] I held as to the nature of the parasite of Kala Azar, that it was a piroplasma; further and closer study of the flagellates has convinced me of my error in the localization of the organism in the group, sporozoa.

I may be premature in abandoning the piroplasma theory, since my knowledge of the piroplasmata of cattle and dogs is not very extensive nor, as far as I understand, has the recent work on the life history of the piroplasmata added very much in elucidation of the cycle undergone by these organisms, especially that portion taking place in the tick.

The very recent discovery, by Mesnil and Brimont,[10] of a flagellate (Endotrypanum Schaudinni) in the red blood corpuscles of an Edentate (Cholœpus didactylus), brings these organisms in very close relationship to the piroplasmata.

II. *The Mode of Transmission of the Disease.*—The mode of transmission of this ailment is still doubtful; Patton[12] has, however, made a step in this direction by finding flagellate forms of Leishmania in the gut of the common bed bug (Cimex rotundatus) of Madras. These insects he fed on severe cases of Kala Azar, in which the parasites existed in large numbers in the peripheral blood stream; but he was successful in only one case, as well as I recollect. Further attempts he made last year in this direction were not successful. I have on several occasions tried to confirm Patton's find by feeding the bed bugs on Kala Azar patients but have not up to the present met with any success.

According to Patton, the patient must be *in articulo mortis*, and the parasite present in large numbers in the peripheral circulation in the wandering endothelium cells, to the extent of 100 and more in one slide, to succeed in this bug-feeding experiment.

Such suitable subjects I have had on three different occasions, but have found no change in the forms of Leishmania ingested by the Cimices even after a week and ten days. Patton has shown me the slides containing the smears of the gut contents of the bugs in which he found the development forms; in these I can confirm the presence of flagellates similar to those obtained in the citrate of sodium solution of Rogers, that is, organisms identical

[5] Chatton and Alilaire. Co-existence d'un Leptomonas (Herpetomonas) et d'un Trypanosoma chez un muscide non vulnèrant, Drosophila confusa, Staeger. Comptes rendus de la Société de Biologie. Tome LXIV, 1908, p. 1004.

*H. muscæ-domesticæ is not biflagellate as Prowazek[11] has attempted to make out, those with two flagella are dividing forms and such individuals are by far the most common kind met with in the gut of some Musca domestica.

[6] Bütschli. Protozoa. Bronn's Klassen und Ordnungen des Tierreichs. Band I, 1880-1889.

[7] Chatton and Alilaire. *Vide* 5 *supra.*

[8] Laveran and Mesnil. Sur un Protozoaire nouveau (Piroplasma Donovani, Lav. et Mesn.) parasite d'une fièvre de l'Inde. Comptes rendus de l'Academie des Sciences. Tome CXXXVII, 1903, p. 957.

[9] Donovan. Human Piroplasmosis. Lancet. 10th September, 1904, p. 744.

[10] Mesnil and Brimont. Sur un Hèmatozoaire nouveau (Endotrypanum, n. gen.) d'un Edenté de Guyane. Comptes rendus de la Société de Biologie. Tome LXV, 1908, p. 581.

[11] Prowazek. Die Entwicklung von Herpetomonas, einem mit den Trypanosomen verwandten Flageilaten. Arbeiten aus dem Kaiserlichen Gesundheitsamte. Band XX, 1904, p. 440.

[12] Patton. Development of the Leishman-Donovan parasite in Cimex rotundatus. Scientific Memoirs by the Officers of the Medical and Sanitary Departments of the Government of India, Nos. 27 and 30, 1907.

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with the flagellates belonging to the genus herpetomonas. I have examined over 200 bed bugs, procured at random, in Georgetown and the Hospital but found no flagellates of any description in their guts; hence it may be stated, from this very limited experience, that a flagellate and particularly the genus herpetomonas, is not a natural parasite or rather commensal of the bed bug of Madras.

Other bugs or rhynchota, congeners of the domestic bug or cimex, both plant feeding and predatory, harbour flagellates of the genera herpetomonas and crithidia. The plant feeding containing the former and the predatory the latter genus. I have found them commonly present in the gut contents of members of the families, reduviidæ and pentatomidæ and Patton in lygæidæ and hydrometridæ.[13] Hence at present, Patton's view concerning the transmission of Kala Azar by bed bugs cannot be accepted in its entirety; that is to say, the herpetomonads he found in the gut contents of Cimex rotundatus may be only the natural commensals of this insect; if so, it must be admitted that they are of very infrequent occurrence as such.

In some of the plant frequenting rhynchotes the forms of herpetomonas were almost identical in all details with Leishmania Donovani, both as found in the human body and in the flagellate stage in Rogers' citrate solution, facts I have mentioned before when discussing the nature of the parasite.

Being dissatisfied with my attempts in bringing about an infection of Cimex with Leishmania and procuring the flagellate forms, I searched for some other blood-sucking insect of local distribution and not so universally spread as the ubiquitous bed bug, and at the same time commensurate in its range with the occurrence of Kala Azar. In my search I came across an insect answering one of the two above desiderata and, although, up to the present, I have not met with any success in propagating, much less transmitting, Leishmania by its means, I consider the find may be an interesting factor in the causation of some disease not necessarily Kala Azar. The insect in question is a black and red bug (Conorrhinus rubrofasciatus, de Geer) of large dimensions, about 20 to 25 millimetres, or, roughly speaking, about an inch in length; it comes occasionally to the light of a lamp into rooms at nights and appears to be widely spread in Madras. (Plate I, Fig. 8.)

It is popularly supposed to suck the blood of human beings and also to feed on the common bed bug; from its latter propensity it is called, according to some of my informants, the "mother of bugs," on account, I suppose, of her unmatronly habit of devouring her smaller relations. This predatory habit on bed bugs is also attributed to its European representative, Reduvius personatus,[14] so a certain amount of credence is to be placed on one of the above popular statements of its habits. Both the male and female insects I have captured contained either fresh or digested mammalian blood in their guts, whether human or not I regret I am unable at present to determine; but hope to procure the opinion of a bacteriologist at some subsequent date.

These bugs readily suck human blood when placed, confined; in either a glass-bottom box or test tube, on the body of a person; they insert their proboscis and begin to suck as if to the manner born. Both the male and female imagines suck human blood; but the nymphs are much more bloodthirsty, starting to insert their probosces immediately they are placed on a patient, while the adults take a minute and more before they settle down to a meal. In the gut of the adult insects, in nearly 90 per cent, large numbers of flagellates of the genus Crithidia are found but no Herpetomonas.

This reduviid bug has a wide distribution both in and out of India, Distant, in the Fauna of British India Series, Rhynchota, Vol. II, p. 286, gives the following habitats:—Sylhet, Bombay, Borghat, Calcutta and Mysore. Ceylon, Andaman Islands, Burma, Toungoo and Mandalay. Outside India it is widely spread throughout the Malayan Peninsula and Archipelago; recorded from Madagascar, West Africa and generally found in the Southern Nearctic and Northern Neotropical regions and in the Antilles.

As mentioned before this insect's habits are nocturnal; both the male and female, the former more frequently, fly into the verandah or room attracted by light. It is found all the year round and I have procured specimens from all parts of the city of Madras.

A strange and interesting coincidence is Darwin's account of a species of the same genus, found in the Pampas district in South America; I quote from his "Voyage of the Beagle" (page 330 of the 1873 edition).

"We slept in the village of Luxan, which is a small place surrounded by gardens and forms the most southern cultivated district in the province of Mendoza, it is five leagues south of the capital. At night I experienced an attack (for it deserves no less a name) of the Benchuca, a species of Reduvius, the great black bug of the Pampas. It is most disgusting to feel soft wingless insects, about an inch long, crawling over one's body. Before sucking they are quite thin, but afterwards they become round and bloated with blood and in this state are easily crushed. One which I caught at Iquique (for they are found in Chili and Peru) was very empty. When placed on a table and, though surrounded by people, if a finger was presented the bold insect would immediately protrude its sucker, make a charge, and, if allowed, draw blood. No pain was caused by the wound. It was curious to watch its body during the act of sucking, as in less than ten minutes it changed from being as flat as a wafer to a globular form. This one feast, for which the benchuca was indebted to one of the officers, kept it fat during four whole months; but after the first fortnight it was quite ready to have another suck."

Darwin's insect belongs to the species C. infestans, Klug (renggeri, Herrich-Schäffer).[15] It is called wing-

[13] Patton. The Life Cycle of a species of Crithidia, parasitic in the intestinal tract of Gerris fossarum, Fabr. Archiv für Protistenkunde. Band XII, 1908, p. 131.

[14] Westwood. Modern Classification of Insects, Vol. II, 1840, p. 472.

[15] Distant. Rhynchota, Vol. II, 1904, p. 285. Fauna of British India.

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less, so it was evidently the nymphs he was dealing with, the adults being winged. It is similarly the case with C. rubrofasciatus; adults suck but they are not so voracious as the nymphs nor do the former become globular from sucking. No ill effects apparently follow the sting of Darwin's insect but in the case of C. sanguisuga in Arizona,[16] great pain and inflammation ensue and may end in the gathering and discharge of pus. Several species of Reduvius attack man in Southern Europe and are frequently met within houses.

Nicolle[17] has last year implicated the ectoparasites of dogs at Tunis as transmitters of the disease, that is, if this Infantile Splenomegaly of his is caused by the same species of Leishmania as Kala Azar.

From the description there is no apparent morphological difference between L. Donovani and his L. infantum. His theory as to the part taken by the dog louse or flea is founded on very slender evidence; to wit, that the children who were affected played with dogs; this it must be admitted is a very much of a *post hoc* argument. On the other hand, what strengthens his opinion is that the stray dogs of Tunis are infected with Leishmania; he examined 145 of these animals and found that 3 harboured the parasite. So it is to be presumed a common transmitter for the dog and the human being is to be looked for. Or, may it not be that the dogs, presumably of the pariah class, fed on recent corpses dead of Infantile Splenomegaly? I have not had an opportunity of examining the pariah dogs of Madras, but intend to do so next April, when the dog-killing operations begin in our city.

III. *Diagnosis of the Disease.*—Clinically this disease is not always easy to diagnose, especially in the early stages, and I have on several occasions, at the first hasty look at patients on admission into my wards, mistaken tuberculosis of the lungs and chronic malaria for Kala Azar.

Again some of the initial cases with pyrexia bear a very close resemblance to typhoid fever. The symptoms of the disease are so protean that nearly all admissions for fever of long duration are suspected to be Kala Azar, for patients sent in for dysentery, diarrhœa, ascites and pneumonia may be and are wrongly diagnosed until time corrects the previous error.

In all chronic cachectics with history of fever the hand is invariably placed over the splenic area to detect an enlargement of the viscus. But it must be remembered that the spleen is not always enlarged; in about 2 per cent. there is no increase in its bulk.

Splenic puncture would clinch the diagnosis but I have abandoned this procedure on account of the risk undergone. I have had three deaths in 170 punctures and further attempts at such operations are, in my opinion, unjustifiable. It is only in patients on the point of death, *i.e.*, a few minutes before the last breath is drawn, that I attempt to puncture the spleen and then only for the growth of Leishmania in artificial media. The finding of the Kala Azar parasite in the peripheral circulation is easy if the observer knows anything of microscopical work and the blood smear is correctly made. My second and third year students after their first week of instruction in the microscope and blood examination find Leishmania with no unusual difficulty.

For the past twelve months particular attention has been paid to the examination of the peripheral blood of Kala Azar patients and, in 93·22 per cent. of all cases, both mild and severe, the parasite has been found in this situation either in the polymorphonuclears or in the mononuclears. The largest number in one slide, and that at the extreme edge only, was 281 and in two other cases over 100 were detected at the marginal end of the blood smear on a single slide.

As it is important to discover the cause of the disease with as little inconvenience and danger to the patient as possible, I may be permitted to go into some detail with reference to the procedure I adopt in obtaining positive finds in such a large percentage. The secret is the formation of the blood smear. A finger of the patient is taken, the tip washed with water and then dried with a towel, the finger is compressed below the pulp for half-a-minute so as to allow as many leucocytes as possible to exude in the drop of blood obtained by the prick of a new pin, one not used before. A needle's prick does not give enough blood and the employment of a surgical needle is barbarous. A small drop of blood, about the size of a large pin's head, is taken up by a slide near its end and a smear made of it by another slide passed slant-wise over it.

The main object is to have the smear end in a straight edge at the finish. All that is necessary is to examine, of course, after fixing and staining the film, this edge, here everything of importance in the smear is located, the leucocytes and any Leishmania that may be present in them; in ten minutes the whole of the contents of the drop of blood are ascertained. Some training is necessary to procure perfect slides of this nature. The slide with which the smear is made, should have a perfectly smooth-ground edge to obviate 'tailing' at the finished margin. It is by neglect of making smears of this kind that success does not attend the endeavours of other observers in detecting Leishmania in the peripheral blood. I do not profess to find the organism in 93·22 per cent. of the cases in a single slide every day, sometimes five slides have been examined on five different, not necessarily successive days, before meeting with success. Out of 59 admissions for Kala Azar last year, 55 gave positive results, 3 negative and one died before the peripheral blood could be examined, *i.e.*, the patient was admitted in the afternoon and died the same night before I could see him the following morning. On the average about two slides were examined on two different days to give the percentage obtained. The cases were not selected, they were all those admitted into my wards indiscriminately, some of a mild type, others again severe, in other words all those diagnosed clinically as Kala Azar. I am sure, however, I am missing the parasites in the very early cases, say those of a month's duration. In cases with high fever and those with complications like broncho-pneumonia, and,

[16] Sharp. Insects. Cambridge Natural History, Vol. VI, 1899, p. 559.

[17] Nicolle and Comte. Origine canine du Kala Azar. Bulletin de la Société de Pathologie Exotique, Tome I, 1908, p. 299.

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on the other hand, such debilitated individuals suffering from dysenteroid or diarrhœic motions, the presence of Leishmania is fairly manifest, 4 or 5 occurring in a slide; then again, *in articulo mortis* large numbers may be present, up to 20 or 30 in a slide.

It is only exceptionally that over 100 are found. Out of the 59 admissions last year, in 3 cases were such large numbers found; in one, as mentioned, as many as 281. The parasite is always included in the white blood cells; in pyrexial in the cytoplasm of the polymorphonuclears and in diarrhœic cases in that of the macrophages of endothelial origin from the spleen or bone marrow. The largest number of Leishmania in one macrophage was 30; here they appear to be in a perfect condition and stain well; it is the reverse in the case of those included in the cytoplasm of the polymorphos, where they are apparently acted on by the ferments of these cells. I have never discovered the Kala Azar parasite in the cytoplasm of the lymphocytes or eosinophiles. Patton[18] states that he has found one in an eosinophile, but I am sure this must be an error as I have particularly sought for them in vain in these cells for the last 18 months, in the blood smears of well over a hundred cases from all sources, from puncture of the spleen, borings from the red bone marrow and from the peripheral circulation. I have recently adopted a new means of procuring Leishmania from the human body during life, and that is by boring into the head of the tibia or into the osteal portion of the ribs by means of a small gimlet. The patient is anæsthetised, either by ethyl chloride or chloroform, a slight incision made over the selected area, the bone exposed and a small portion of red bone marrow removed by an ordinary gimlet. Marrow from the head of the tibia is not so satisfactory but that from the ribs contains Leishmania in large numbers, closely packed in the endothelial cells of the myeloid tissue. The forms appear to be in a fresher condition, if I may be allowed to make use of a loose expression, but there is no change in the morphology of the organisms, no attempts at growth or any signs of the origin of the flagellum. I undertook this innovation to find out forms of the parasite possessing some manifestations of activity in giving rise to pyrexia and the other signs of *mal être* common to the disease, as it is hard to understand how the usual inert apparently encysted looking forms of Leishmania could give rise to active symptoms. I have mentioned in a previous contribution, the peculiarity of the leucocytes in Kala Azar. A knowledge of this fact is of considerable help in the diagnosis of the disease from malaria and typhoid fever, types of fevers having mononucleosis as a common characteristic. In advanced cases of Kala Azar leucopenia is marked, more so than in any other ailment that I am acquainted with; along with this there is a relative increase of the mononuclear type of leucocytes. The polymorphos are considerably changed as far as the appearance of their nucleus and cytoplasm is concerned. The granulations of the cell are diminished if not entirely absent; the nucleus loses its apparent polynuclear nature, becomes band or ribbon-shaped instead of possessing the normal strings connecting the different thickened nuclear masses. Another feature in the change of the nuclei of the polymorphonuclears is the presence of very small buds or beads on short thin pedicles attached to different parts of the nuclear substance. These peculiarities are not limited to cases of this disease, but are very much more evident than in any other ailment showing a mononuclear type of blood change. The presence of endothelium cells too is characteristic; some of these may be passed off as transition mononuclears. Division forms are common among these cells, the nucleus divides into two or more portions connected by a very slender nuclear string, taking on in others a marked polynuclear character. Occasionally beautiful mitotic figures are met with. The second plate attached shows better than any description the peculiarities alluded to. The red blood corpuscles are invariably much reduced in number, about an average of 2,500,000 to the cubic millimetre; the blood is consequently less viscous and blood smears can be very much more satisfactorily prepared than with the normal and more viscid blood. This is a fact worth remembering and a help in diagnosis. Owing to the paucity of the polymorphonuclear leucocytes the blood coagulates very slowly; and a drop of blood from a single pin-prick may be repeatedly pressed from the finger for nearly five minutes.

(*IV*).—*Attempts at cure, by* (*a*) *drugs*, (*b*) *by bringing on inflammation and* (*c*) *by change of residence.*—(*a*) I cannot state that the drugs I have tried have had any beneficial and lasting effect. Among some of the number, I may mention the various salts of quinine in large doses, both by mouth and intramuscular injection, *ad nauseam*; Liquor Arsenii et Hydrargyri Iodidi, with and without Vinum Antimonniale; Fuchsine and latterly Thymol dissolved in rectified spirits. At first I was under the impression that Fuchsine was giving satisfactory results but I have now changed my opinion. The amelioration was transitory. A single patient, a boy of about 14 years old, was the only exception: he was persuaded to stay in hospital for six months and took 1c.c. of a 20 per cent. solution of Fuchsine three times a day during this long period. He is now, 18 months after, in perfect health and is working in my laboratory at the hospital. The other physicians here have tried X-rays, Atoxyl and Soamin, but no marked change has resulted from such treatment.

(*b*). *By bringing on inflammation.*—I have had a cure of another patient after a very severe attack of cancrum oris and in the wards of the Fourth Physician, Capt. E. W. Browne, I.M.S., a patient is on a fair way to recovery after facial erysipelas.

(*c*). *Change of residence.*—"Change of air, especially "to a dry hot climate, appears to bring about a cure in "some of the cases. A few of my old Kala Azar patients "have returned to see me, restored to health and appa- "rently quite well. I may mention such places in our "Presidency, answering to suitable sanatoria (if I may

[18] Patton. Development of the Leishman-Donovan parasite in Cimex rotundatus. Scientific Memoirs by the Officers of the Medical and Sanitary Departments of the Government of India, No 30, 1907, p. 3, and Plate 3.

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"use the expression) for Kala Azar; to wit, Kurnool, "Cuddapah and Anantapur." I made this statement in our General Hospital Report for 1907. Since then I have sent two patients to Cuddapah, one of them returned after a month with but slight improvement and the other, after a three months' stay there, returned to his native place very much the worse for the change; he suffered all the time he was at Cuddapah, with the most marked intermittent rises of temperature I have known in Kala Azar, the temperature ranging from normal to 105° F. and occurring twice a day. Both these patients have since died.

EXPLANATION OF PLATES.

All the figures, with the exception of No. 8, have been drawn by means of Abbe's Camera lucida and Zeiss's Apochromatic Objective 2 mm., num. apert. 1·40 and No. 12 Compensation Eye-piece. The surface of the drawing paper was 430 mm. from the prism of Abbe's apparatus, giving a magnification of 2,580 diameters. The staining was the author's modification of Jenner.

PLATE I.

1. Herpetomonas muscæ domesticæ, Burnett.
2. Herpetomonas (Leptomonas) lygæi, Patton.
3. Herpetomonas (Leptomonas) inhospes, sps. nov.
4. Leishmania Donovani, Laveran and Mesnil, from citrate of sodium solution.
5. Crithidia Conorrhini, sps. nov.
6. Trypanosoma Evansi, Steel.
7. Herpetomonas (Leptomonas) sarcophagæ? Prowazek, showing the gradations in the localisation of the blepharoplast from the anterior to the very posterior end of the body of the flagellate.
8. Conorrhinus rubrofasciatus, de Geer. Male and female, natural size.

PLATE II.

Cells in the peripheral blood.

9. Two polymorphonuclear leucocytes, showing the band or ribbon-shape of the nucleus and the small buds or beads on short thin pedicles. The granulations in the cytoplasm are diminished in number.
10. A polymorphonuclear leucocyte with 4 Leishmania in its cytoplasm.
11. A normal polymorphonuclear showing the strings connecting the 4 thickened nuclear masses, the granulations are much more numerous than those shown in the preceding 3 polymorphos.
12. An endothelial cell, the nucleus divided in two.
13. An endothelial cell with a stalked bead attached to its nucleus.
14. An endothelial cell the nuclear lobes connected by a very slender cord.
15. An endothelial cell showing mitotic figure.
16. An endothelial cell the nucleus having a very marked polynuclear appearance.
17 & 18. Endothelial cells with 6 and 30 Leishmania Donovani in their cytoplasm. The red cells in the proximity are red blood corpuscles.

DISCUSSION.

Major Rogers said:—As long ago as 1897 I pointed out the marked reduction in the number of the leucocytes in the blood of kala-azar patients, and have since found it to be the most constant and characteristic change in uncomplicated cases of this disease, and one which is of the greatest diagnostic and prognostic value. The loss is chiefly one of the polynuclears, which are commonly only from one-tenth to one-twentieth of the normal numbers, the death-rate being in proportion to the degree of their destruction. I have previously drawn attention to the remarkable recoveries which sometimes follow septic complications such as cancrum oris, but only when a marked increase of the total polynuclears occurs. As I also found cancrum oris in these cases to be accompanied by a general staphylococcus infection, which sometimes appears to produce a disappearance of the parasites of kala-azar from the internal organs I suggested and used a vaccine made of these organisms killed at 60 C, in accordance with Sir A. E. Wright's methods, and recorded in my work on Fevers in the Tropics that this method of treatment had in several cases appeared to be of undoubted value. During 1908 I have been able to further test this method, thanks largely to the kind permission of Lieutenant-Colonel Harris, I.M.S., to try it on cases in his wards at the Calcutta Medical College Hospital. The accompanying table (*see page* 165) includes all the uncomplicated cases so treated during the past year, being thus a consecutive series of unselected cases, which furnish the basis for the following observations.

Blood counts were made by myself before the vaccine was used, and again before subsequent doses, which were usually given at the intervals of from a week to ten days. One hundreth of an ordinary agar slop culture of a staphylococcus, originally obtained from a cancrum oris case of kala-azar, was contained in 2½ minims of the stock vaccine (about 250,000,000 cocci) and the doses rapidly increased from 2½ to 10 minims or more. The increases of the leucocytes noted were thus present from 7 to 10 days after the previous dose of vaccine had been subcutaneously injected, either in the upper arm or over the spleen, so that they represent more than the immediate effect of each dose. In addition to the counts of the red and the white corpuscles (which furnish data for calculating the ratio of the white to the red corpuscles), I also made a differential count in most of the cases, so that the actual increase in the total polynuclears could also be estimated as shown in the table.

Effect on the number of Leucocytes in the Blood.—The first noteworthy feature is the marked increase in the total number of the leucocytes which followed the injections in 12 of the 14 cases, although in two, namely Nos. 6 and 15, it was unfortunately only temporary in nature, the numbers subsequently declining again. Of the remaining two, in No. 1 a slight temporary total increase, without any rise in the total polynuclears, was obtained, while in No. 7 no increase followed the single small dose observed. In the great majority of the cases, then, a marked leucocyte increase was obtained and was accompanied by a rise in both the proportion of the white to the red corpuscles and in the percentage and total numbers of polynuclears, which is the desired result.

The General Effects of the Treatment.—As the patients were all natives, who could not be kept in hospital for long periods, only the immediate general effects can be recorded. Some were not long enough in hospital to allow of much permanent good being effected, while No. 3 contracted dysentery and died. The majority, however, showed distinct signs of improvement, the temperature declining to a very low intermittent form or to normal, and weight being gained. The results, as a whole, were certainly better than by any other treatment I have seen tried in these very unsatisfactory cases. The patients were all in an advanced stage of the disease, so that earlier and more persistent trials of this treatment seem to be indicated, especially as it can be used in addition to any drugs, which may be considered of value.

Capt. Foster said that no satisfactory method for diagnosing the affection had hitherto been demonstrated. He had failed to find the parasites in peripheral blood in 1000 blood films examined by him, and it was curious that the results at Madras and Murshidabad had so markedly differed.

Mr. Ramchandariar referred to his observations at Madras, Mysore, etc. He criticised the attitude of specialist observers whose sole attention was devoted to but one single subject to the total exclusion of all others: in fact their imagination ran riot and they were simply mad after one thing and one alone, apparently oblivious of the fact that other things and subjects existed in nature, and that theirs was but an insignificant fragment of the whole.

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No.	Race.	Sex.	Age.	Date of Vaccine.	Dose of Vaccine.	Date of Blood Exam.	Red Corpuscles.	White Corpuscles.	Ratio red to white.	Total Polynuclears.	Percentage Polynuclears.	
1	H.	M.	21	11-3	5 Min.	11-3	3,600,000	2,875	1-1,254	1,874	65·2	Fever on.
...	...	...	...	20-3	10 „	20-3	3,880,000	3,500	1-1,109	1,643	47	
...	...	...	...	...	...	25-3	.....	3,125	...	1,663	53·6	Fever much lower. Improved.
2	Nt. Ch.	M.	18	23-2	5 Min.	22-2	2,465,000	625	1-3,944	369	59	
...	...	...	...	5-3	7½ „	4-3	4,420,000	3,125	1-1,414	2,081	65	
...	...	...	...	14-3	7½ „	14-3	3,220,000	3,625	1-1,226	1,286	49	Very much improved. Temperature normal.
3	H.	F.	12	5-3	5 „	4-3	3,430,000	2,125	1-1,614	1,126	53	
...	...	...	...	15-3	5 „	15-3	2,760,000	6,375	1- 440	4,692	73·6	Much improved. Temperature normal.
...	...	...	...	...	...	...	3,190,000	6,250	1 510	4,700	75·2	Subsequently died of dysentery.
4	H.	M.	30	10-3	5 Min.	7-3	4,200,000	2,875	1-1,460	2,085	73·2	
...	...	...	...	...	...	19-3	4,260,000	12,000	1- 355	7,488	82·4	Much improved. No fever.
5	E.	F.	17	2-4	5 Min.	1-4	3,880,000	2,875	1-1,348	1,035	36	
...	...	...	...	10-4	7½ „	10-4	2,820,000	4,000	1- 705	2,080	52	Much improved. Temperature normal.
6	E.	F.	45	24-3	5 „	23-3	2,770,000	1,500	1-1,847	1,284	85·6	
...	...	...	...	31-3	7½ „	31-3	3,490,000	3,375	1-1,016	2,916	86·4	
...	...	...	...	7-4	7½ „	7-4	2,930,000	1,375	1-2,131	976	71	No improvement, died of Pneumonia later.
7	M.	M.	12	27-5	2½ „	27-5	2,105,000	2,125	1- 982	...	...	
...	...	...	...	5-6	5 „	5-6	2,505,000	1,875	1-1,322	...	...	No improvement, lost weight.
8	E	F.	30	28-4	5 „	15-4	2,500,000	1,500	1-1,667	870	58	
...	...	...	...	8-5	7½ „	8-5	2,860,000	2,750	1-1,040	1,432	63	
...	...	...	...	16-5	10 „	16-5	2,815,000	1,875	1-1,301	...	...	
...	...	...	...	16-6	10 „	16-6	2,705,000	1,250	1-2,164	...	...	No increase of Leucocytes.
...	...	...	...	2-7	15 „	2-7	2,880,000	1,625	1-1,754	...	...	Gained in weight, slight improvement.
9	Nt. Ch.	M.	17	29-4	5 „	29-4	4,130,000	2 250	1-1,613	1,192	53	
...	...	...	...	7-5	7½ „	7-5	3,150,000	3,125	1-1,008	1,651	53	No change.
10	H.	M	12	5-7	5 „	5-7	2,580,000	1,250	1-2,069	...	...	
...	...	...	...	14-7	7½ „	14-7	3,735,000	2,500	1-1,490	1,350	54	Improved. Temperature normal.
11	H.	M.	24	30-1	2½ „	22-1	3,730,000	3,375	1-1,105	796	23·6	
...	...	...	...	14-2	5 „	14-2	3,860,000	7,750	1- 498	1,116	14·4	
...	...	...	...	11-3	7½ „	11-3	3,714,000	1,250	1-2,968	237	19	
...	...	...	...	25-3	10 „	20-3	4,120,000	1,875	1-2,197	1,143	61	
...	...	...	...	4-4	10 „	4-3	4,520,000	4,000	1-1,130	2,250	57	
...	...	...	...	11-4	10 „	11-4	4,060,000	5,000	1- 812	3,000	60	Greatly improved and gained weight. No fever.
12	H.	F.	22	5-11	10 „	4-11	2,350,000	2,375	1- 984	...	...	
...	...	...	...	...	...	16-11	2,420,000	3,500	1- 691	2,296	65·6	Improved. No fever.
13	M.	M.	38	11-11	2½ Min.	11-11	2,190,000	3,000	1- 730	...	...	
...	...	...	...	23-11	5 „	23-11	2,220,000	6,000	1- 370	3,168	52·8	
...	...	...	...	30-11	7½ „	30-11	2,345,000	6,750	1- 348	...	...	Much improved, gained weight.
14	E.	M.	15	...	...	19-12	2,515,000	3,375	1- 745	...	...	
...	...	...	...	23-1	2½ Min.	23-1	2,105,000	2,000	1-1,052	...	...	Worse, vaccine commenced.
...	...	...	...	2-2	10 „	2-2	1,715,000	1,715	1-1,744	...	...	
...	...	...	...	...	...	19-2	2,900,000	5,000	1- 580	...	...	Temperature nearly normal, gaining weight.

Col. Campbell said that vaccine treatment had been very efficacious, and that similar treatment, through the use of issues, &c., has been known to the natives of India for centuries.

Capt. Christophers said that the relation of the Leishman-Donovan parasite to *piroplasma* depended upon the real nature of *piroplasma*. If piroplasma like the malaria parasite was one of the Sporozoa there was no very close relationship.

Both Koch and the speaker had described a number of developmental forms of piroplasma in the tick. None of these bore any resemblance to stages of the Flagellata. On the other hand there were resemblances to stages of the malaria parasite which was a Sporozoa.

Just as in the malaria parasite flagellation occurred as a sexual process, so it might do in piroplasma, and the forms recently described in Liverpool though they had flagella bore little or no resemblance to the flagellata. They were transient forms and had no blepharoplast like that of the flagellates. The flagella were also multiple and very fine. Such forms were quite compatible with piroplasma being a sporozoan. The speaker had called attention to the possibility of a sexual flagellation occurring prior to the formation of the club shaped bodies of Koch which seemed to be analogous to the Oopinite of the malarial parasite.

Major S. P. James said: "In connexion with Major Donovan's statement that he does not now regard the Leishman-Donovan parasite as a Piroplasma, it would be of interest to know his present opinion regarding the forms of the parasite which at one time he described as being present in the red blood corpuscles, but to which he does not allude in the present paper. The omission by Major Donovan of any reference to the parasites of Oriental sore is also of interest as it points to the fact that this disease does not occur in Madras. So far as I am aware no place has yet been found in India where kala-azar and Oriental sore exist side by side. It is unfortunate that more observations relating to geographical distribution have not been made in this country, since such observations are well adapted for settling many problems in connexion with the nature and pathogenic properties of parasites of this class. Sir Patrick Manson's suggestion that the parasites of Oriental sore may be the parasites of kala-azar modified by passage through some animal also still remains untested in India. Such observations on geographical distribution as we possess at present are not unfavourable to the correctness of this view and it would be a remarkable blessing to mankind if by inoculating a person with the parasites of Oriental sore we could protect him against kala-azar."

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Dr. Bently-remarked that it was evident that the disease met with by Major Donovan in Madras and Capt. Foster in Bengal was the endemic form of kala-azar in which cases rarely showed such a rapid course and acute symptoms as in the epidemic form of the disease. The speaker had seen over a thousand cases of kala-azar in an acute epidemic in Assam. This number occurred in a comparatively small population on a tea-garden. Not less than three-quarters of the entire population of two large coolie lines were entirely wiped out during a period of five years.

At the height of the epidemic cases rarely lasted longer than six months after the onset of the disease which decimated whole households. Finally the epidemic ceased as suddenly as it began, and now it was difficult to discover definite cases of kala-azar in the same place in which a few years back hundreds of cases were to be found.

During the waning of the epidemic there appeared to be an extraordinary lessening in virulence, for many cases appeared to recover spontaneously—and the speaker knew of a considerable number in whom the parasite had been found by splenic puncture who were now alive and well and apparently completely recovered. At the height of the epidemic 95 per cent. mortality occurred, but later on 50 per cent. or more recovered. The reason why the disease described by Major Donovan showed a very high mortality was undoubtedly because he was dealing with hospital cases. There must be many hundreds of milder cases, the great majority of whom never went near a hospital and eventually either recovered or died after very long continued infection.

Major Donovan had referred to diagnosis. This was still a very difficult matter. In the speaker's opinion it was practically impossible to diagnose kala-azar clinically except when it was present in the epidemic form in a locality where the medical man seeing the cases had a close personal knowledge of the patients, having been familiar with them bofore the onset of the disease. He would refuse to give a definite opinion upon any case or cases merely presented for his casual inspection however closely they might resemble kala-azar. Some years ago he (the speaker) drew attention to the clinical resemblances between kala-azar and Malta fever. It was an interesting point that, more recently, Bassett-Smith a recognized authority upon Malta fever, had confirmed this striking resemblance after having seen and studied cases of kala-azar. This illustrated the great difficulty of diagnosis from clinical signs.

Major Donovan had referred to the dangers of splenic puncture and the possibility or certainty of finding parasites in the peripheral blood; but his own experience did not correspond with Major Donovan's.

In the first place in close on a hundred spleen punctures he had seen no bad result. A hypodermic syringe (all glass) and a fine needle had always been employed by him. As regards the difficulty of finding the parasite in peripheral blood films his experience coincided with that of Capt. Foster.

One point must be noted however—when late in 1903 after Major Donovan's discovery of the parasite in Madras, he (the speaker) had been successful in finding for the first time the presence of the parasite in cases of kala-azar in Assam—the epidemic was already on the wane. It was quite possible that the difficulty of finding parasites in the peripheral circulation of even very severe cases at this time bore some relation to this fact. The extraordinary way in which the disease disappeared when everything appeared favourable to its spread did not however support the bed-bug hypothesis as to its transmission. As regards treatment, his experience coincided with Major Donovan's—he could not say that he had seen any definite results from any form of treatment. The peculiar course of the disease often misled people, and, as many cases recovered quite apart from treatment, mistakes arose as to the value of certain remedies.

Dr. Pettigara held that kala-azar and Delhi boil were not identical, and that he was prepared to support the views of Major Leonard Rogers from his personal observations.

OBSERVATIONS ON FEVERS IN THE PHILIPPINE ISLANDS.

By Capt. EUGENE R. WHITMORE, M.D.,
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With increase in our knowledge of, and experience with, diseases in the tropics, comes the knowledge that there are comparatively few diseases that are limited to the tropics, and this is especially true of the fevers, so that "Diseases in the Tropics" and "Fevers in the Tropics" seem to have become more appropriate than "Tropical Diseases" and "Tropical Fevers." However, there are some fevers that at present are not known to spread outside the tropics, while some of the cosmopolitan fevers present peculiarities in the tropics that merit special consideration.

It is not my intention to discuss all of the fevers found in the Philippine Islands, as they do not differ from the same fevers as found elsewhere; but it is my desire to note a few points that have interested me during my service here.

Malarial fever is commonly met with and, so far as I know, does not differ from the same disease elsewhere. In about five thousand positive blood examinations in a little over three thousand cases of malaria, I have found the quartan parasite in only twenty-seven cases. In 1,031 consecutive cases of which I have record of the blood finding, the sub-tertian parasite was found alone 661 times; the tertian parasite was found alone 343 times; the two were found together 23 times; and the quartan parasite was found alone 4 times. Crescents were found 73 times. The quotidian parasite does not appear after my first five hundred cases. Two cases of sub-tertian infection developed hemoglobinuria and both died. One case was an American soldier and the other was a native woman.

In one company of Native Scouts examined for malarial infection, 28 men in a company of 101 had malarial parasites in their blood. All of these men were doing duty and only one admitted that he did not feel well.

Dengue fever is common and does not need any discussion.

It is known that typhoid fever is not at all uncommon among the whites as well as the natives in all parts of the Islands where it has been carefully sought for. Whether the incidence of typhoid among the natives has increased since American occupation and the stationing of American troops in various parts of the islands, I cannot answer. In a fairly large experience

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